ORIGINAL RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 7 | July 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Is There a Role of Image Guided Renal Biopsy in the Management of T1 Renal Masses?

KEYWORDS: Image guided biopsy, renal cell carcinoma, percutaneous, small renal masses

Nirmal Thampi John
Associate Professor, Department of Urology, Christian Medical College, Vellore 632004

Amit Deshpande
Senior Registrar, Department of Urology, Christian Medical College, vellore 632004

ABSTRACT *The aim of our study was to compare the outcome of image guided biopsy (IMG) of renal masses ≤ 7cms with final histopathological diagnosis. All study patients underwent CT guided percutaneous biopsy followed by surgery for the renal mass. The pathological characteristic of the IGB and the histopathological specimen were compared, including Fuhrman's grading. Out of 25 biopsies, 20 biopsies showed clear cell RCC, and corresponded with final histological outcome. However, of the 3 patients who were reported to have hybrid oncocytic variant on IGB; 2 had oncocytoma and the third had chromophobe RCC. 2 samples were inadequate for interpretation. Sensitivity, specificity, PPV, and NPV for the detection of malignancy by IGB were 92%, 100%, 10% and 33% respectively. The accuracy of the core biopsy was 100%; however the accuracy for the differentiation of Fuhrman grade was 76% only.*

Introduction

In recent years, 48 to 66% of Renal cell carcinomas (RCCs) have been detected incidentally as small renal masses (SRMs) in asymptomatic patients (1). 30% of tumours below 4 cm in their maximum dimension were benign and over 87% of those diagnosed as clear-cell RCCs were low-grade tumours (2). An analysis of the Surveillance Epidemiology and End Results (SEER) database from 1998 to 2003 showed a 5.2% prevalence of metastasis at presentation among 8792 patients with RCCs ≤4 cm, with an increase of metastasis by 3.5% for each 1-cm increase in tumour size (3). Although most contrast-enhancing renal masses are malignant, CT or MRI features fails to conclusively differentiate RCCs from benign tumours such as oncocytomas and "low fat" angiomyolipoma (4,5). These observations have led to the development of alternative treatment options for selected patients with SRMs, e.g. minimally invasive ablative therapies and even active surveillance (AS). To this end, image-guided biopsy (IGB) could provide information that may be helpful when deciding on the most appropriate management strategy for these patients.

Material and methods

The aim of our study was to compare the outcome of imaging guided biopsy (IGB) of renal masses with final histopathological diagnosis, including Fuhrman's grade in case of malignancy. We aimed to calculate sensitivity, specificity positive predictive value and accuracy of IGB in determining the diagnosis. Secondary outcomes included assessing the complications secondary to IGB and effect of nephrometry score on biopsy outcome.

This prospective study was carried out over one year after approval from the Institutional review board and Ethics committee. All patients with renal masses of size ≤7cms (T1) were included after an informed written consent. Patients with metastatic disease, renal vein/ Inferior vena cava thrombosis at presentation and those with deranged coagulation profile were excluded. Sedoanalgesia was given prior to biopsy. The patient was placed in the prone position, and 1% lignocaine local anesthesia was used. Under Computed tomography guidance, a coaxial technique was used for biopsy using an 18 gauge needle. The biopsy was processed by a dedicated uro-pathologist. Post biopsy, patient's vital signs were monitored at regular intervals to rule out any occult bleed, trauma to surrounding organs like pleura, liver, colon, spleen. Irrespective of the biopsy report these patients underwent a radical/ partial nephrectomy.

Results

A total of 25 biopsies were carried out during the study period. The mean age of the patients was 48 yrs (median: 51 yr; range: 28–83 yr). 56% percent of renal masses were incidentally detected.

Table-1 Demographic profile (n= 25)

Mean Age		48.8 yr
Sex (%)	Male	21 (84)
	Female	4 (16)
Side (%)	Left	14 (56)
	Right	11 (44)
Co morbidities	DM	8
	HT	11
	CKD	4
	Other	13
Presentation (%)	Non specific Flank pain	4 (16)
	Hematuria	4 (16)
	Other	3 (12)
	Incidentally detected during routine evaluation	14 (56)

DM- Diabetes Mellitus; HT- Hypertension; CKD- Chronic Kidney disease

Mean tumour diameter on pre-operative CT scan was 4.1 cm (median: 3.2 cm; range: 2.2-7cm). About 68% tumours had size ≤ 4 cms. Post-operatively however, about 88% tumours were reported as pT1a suggesting that the CT overestimates the size of tumour.

Out of the 25 core biopsies, 20 biopsies showed clear cell RCC, which also corresponded with final histological outcome. Three patients were reported to have hybrid oncocytic variant, out of which 2 had oncocytoma and the third one turn out to be chromophobe RCC. Two IGB samples were inadequate for interpretation; the final histopathology revealed lipid poor angiomyolipoma and clear cell RCC respectively. Out of 25 core biopsies, 22 patients had malig-

Volume : 6 | Issue : 7 | July 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

nancy in final histological analysis. One IGB biopsy which was inadequate for reporting was also found to have RCC. Of the three patients in whom IGB revealed hybrid oncocytic tumour, one was eventually reported as chromophobe RCC.

Table-2 Diagnostic accuracy of Image guided biopsy

Insufficient	2
Detection of malignancy (accuracy)	100%
True-positive, *n*	20
False-negative, *n*	1
False-positive, *n*	0
True-negative, *n*	2
Sensitivity	95%
Specificity	100%
PPV	100%
NPV	66%

PPV- positive predictive value; NPV- negative predictive value

Of the 20 patients where IGB revealed RCC, subtype was correctly predicted as clear cell in 100% patients. However the accuracy for the differentiation of Fuhrman grade was only 75%. IGB failed to identify Fuhrman grade 3 in 1 patient and in 4 patients, where the IGB grade was I, the final histological outcome showed Fuhrman grade II.

5 patients reported biopsy site pain (VAS < 4) which settled with oral analgesics. One patient developed localized hematoma at biopsy site and another required hospitalisation for monitoring of hematuria. Both of them settled with conservative measures.

Discussion

Renal mass biopsy is most often done under image guidance. The potential disadvantages of US include the inability to differentiate iso-echoic renal masses from normal renal parenchyma, distinguishing adjacent pleural folds and bowel. Technical difficulties include biopsying in the obese population (6).

All these problems can be avoided using CT fluoroscopy. The advantages of CT guidance are that 1] gas and other structures do not obscure visibility, 2] there is excellent spatial resolution, 3] there is better needle visualization, 4] it is easier to avoid necrotic areas and 5] there is more rapid skill acquisition. 6] It also provides a higher resolution image and thereby facilitates the avoidance of adjacent vital structures and necrotic areas at the time of sampling. In the present study, all biopsies were done under CT guidance. We were able to obtain adequate sample in 92% cases. By using CT fluoroscopy, which allows biopsy gun activation in real-time mode, Neuzellet *et al* (7) discovered that in some cases the needle pushes the tumour instead of penetrating it. This phenomenon could explain the high failure rate in small tumours observed in studies where fluoroscopy is not used.

The reported sensitivity of biopsy for the diagnosis of malignancy ranges from 80% to 92%, regardless of the needle size used or whether the specimens were examined cytologically, histologically, or both (8). False-negative results are most often due to a failure to place the needle tip accurately in a small mass. In the current study only about 8% of percutaneous biopsies showed false-negative results. Exciting advances in immunocytogenetics and the emergence of reliable markers for identifying specific renal neoplasms, hold great promise for image guided biopsies (9) . These analyses have the potential for reducing the incidence of non-informative biopsies and providing increased differentiation of "oncocytic neoplasms".

One example of this is the study from Beland *et al* who analyzed biopsies that were non-informative by conventional hematoxylin-eosin staining alone, and reported a definitive diagnosis in 89% of cases with the addition of immunohistochemistry and other ancillary techniques (10). The major diagnostic challenge is represented by oncocytomas. Oncocytic cells are found in numerous RCCs, such as chromophobe RCC, the granular cell variant of RCC, and the eosinophilic variant of papillary type RCC (type 2). Immunocytochemistry can help to distinguish between RCC and oncocytomas. In this series, 1 of the 3 patients in whom oncocytic neoplasm was diagnosed on IGB, final histopathology was reported as chromophobe RCC. Angiomyolipomas are considered difficult to identify on biopsy due to nuclear atypia and pleomorphism comparable to those found in RCC (9). However HMB-45 is constantly expressed by angiomyolipomas but not by RCC or liposarcomas. Additionally, angiomyolipomas are negative for cytokeratin (11). In this study so far we have seen only one lipid poor angiomyolipoma in which the IGB was non informative.

We were able to diagnose subtype of renal cancer in 20 of the 22 patients (90%). Barocas *et al* (12) was able to improve the accuracy of sub typing from 90% to 95% by adding molecular diagnosis (real time RNA-PCR) to histopathologic diagnosis. Subtypes of RCC have distinct cytogenetic abnormalities, such as the loss of 3p in clear-cell, trisomy 7 or 17 in papillary, and widespread chromosomal losses in chromophobe RCC (7, 10, 13). A recent study by Gowrishankar B *et al* (14) lends support for a role of a novel FISH assay to assist in the yield and accuracy of diagnosis of renal cortical neoplasms in needle biopsies, in particular to help guide clinical management of patients with SRMs that were non-diagnostic by histology.

Concordance rates between biopsy specimens and final surgical pathology range from 46% to 94% for Fuhrman nuclear grade (15,16). This divergence may be a result of both inter-observer variability and tumour heterogeneity. The significance of this becomes apparent with the increasing use of active surveillance and ablative therapies, which generally should not be utilized in the setting of a high-grade cancer, regardless of size (17).

Neuzillet *et al* (7), investigating 88 biopsies performed with CT guidance and 18-gauge needles in small solid masses, reported a concordance of Fuhrman nuclear grade in percutaneous biopsy and histopathologic specimens of only 69.8%. In our study the accuracy for detecting high and low Fuhrman grade was 75%. Because Fuhrman grade is a prognostic marker, improvements are needed for a better classification of nuclear grade on biopsy specimens.

As a secondary outcome, we tried to see if any there was correlation between renal nephrometry score and biopsies, however, no statistically significant association was found.

Conclusion

The role of IGB in the setting of T 1 renal masses is expanding. In our study, the sensitivity, specificity, PPV, and NPV for the detection of malignancy by core biopsy were

Volume : 6 | Issue : 7 | July 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

92%, 100%, 10% and, 33% respectively. The accuracy of the core biopsy was 100%; however the accuracy for the differentiation of Fuhrman grade was 76% only. Ongoing research continues to show promise in the development of molecular, cytologic and histologic markers to further characterize renal masses and help determine optimal therapy for patients.

References

1. Bosniak MA. Angiomyolipoma (hamartoma) of the kidney: a preoperative diagnosis is possible in virtually every case. Urol Radiol. 1981;3(3):135–42.
2. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: an analysis of pathological features related to tumor size. J Urol. 2003 Dec;170(6 Pt 1):2217–20.
3. Nguyen MM, Gill IS. Effect of renal cancer size on the prevalence of metastasis at diagnosis and mortality. J Urol. 2009 Mar;181(3):1020–7.
4. Kim JK, Park S-Y, Shon J-H, Cho K-S. Angiomyolipoma with minimal fat: differentiation from renal cell carcinoma at biphasic helical CT. Radiology. 2004 Mar;230(3):677–84.
5. Rodríguez-Rubio FI, Díez-Caballero F, Martín-Marquina A, Abad JI, Berián JM. Incidentally detected renal cell carcinoma. Br J Urol. 1996 Jul;78(1):29–32.
6. Remzi M, Katzenbeisser D, Waldert M, Klingler H-C, Susani M, Memarsadeghi M, et al. Renal tumour size measured radiologically before surgery is an unreliable variable for predicting histopathological features: benign tumours are not necessarily small. BJU Int. 2007 May;99(5):1002–6.
7. Neuzillet Y, Lechevallier E, Andre M, Daniel L, Coulange C. Accuracy and clinical role of fine needle percutaneous biopsy with computerized tomography guidance of small (less than 4.0 cm) renal masses. J Urol. 2004 May;171(5):1802–5.
8. Silverman SG, Gan YU, Mortele KJ, Tuncali K, Cibas ES. Renal masses in the adult patient: the role of percutaneous biopsy. Radiology. 2006 Jul;240(1):6–22.
9. Koul H, Huh J-S, Rove KO, Crompton L, Koul S, Meacham RB, et al. Molecular aspects of renal cell carcinoma: a review. Am J Cancer Res. 2011;1(2):240–54.
10. Beland MD, Mayo-Smith WW, Dupuy DE, Cronan JJ, DeLellis RA. Diagnostic yield of 58 consecutive imaging-guided biopsies of solid renal masses: should we biopsy all that are indeterminate? AJR Am J Roentgenol. 2007 Mar;188(3):792–7.
11. Nelson CP, Sanda MG. Contemporary diagnosis and management of renal angiomyolipoma. J Urol. 2002 Oct;168(4 Pt 1):1315–25.
12. Barocas DA, Mathew S, DelPizzo JJ, Vaughan ED Jr, Sosa RE, Fine RG, et al. Renal cell carcinoma sub-typing by histopathology and fluorescence in situ hybridization on a needle-biopsy specimen. BJU Int. 2007 Feb;99(2):290–5.
13. Lechevallier E, André M, Barriol D, Daniel L, Eghazarian C, De Fromont M, et al. Fine-needle percutaneous biopsy of renal masses with helical CT guidance. Radiology. 2000 Aug;216(2):506–10.
14. Gowrishankar B, Cahill L, Arndt AE, Al-Ahmadie H, Lin O, Chadalavada K, et al. Subtyping of renal cortical neoplasms in fine needle aspiration biopsies using a decision tree based on genomic alterations detected by fluorescence in situ hybridization. BJU Int. 2014 Dec;114(6):881-90.
15. Volpe A, Kachura JR, Geddie WR, Evans AJ, Gharajeh A, Saravanan A, et al. Techniques, safety and accuracy of sampling of renal tumors by fine needle aspiration and core biopsy. J Urol. 2007 Aug;178(2):379–86.
16. Schmidbauer J, Remzi M, Memarsadeghi M, Haitel A, Klingler HC, Katzenbeisser D, et al. Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses. Eur Urol. 2008 May;53(5):1003–11.
17. Lebret T, Poulain JE, Molinie V, Herve JM, Denoux Y, Guth A, et al. Percutaneous core biopsy for renal masses: indications, accuracy and results. J Urol. 2007 Oct;178(4 Pt 1):1184–1188; discussion 1188.